

WHAT IS CLAIMED IS:

- 0959764-042700
1. A method for preventing or treating a disorder resulting from release of bradykinin
5 in a mammal, wherein said mammal produces HBP that binds to an HBP antagonist,
said method comprising administering to said mammal in need thereof, a mammalian
HBP antagonist in an amount effective to decrease release of bradykinin in said
mammal.
 - 10 2. The method according to claim 1, in which the HBP antagonist is present in an
amount of from about 10 mg to about 1 g per unit dosage form.
 3. The method according to claim 1, in which the HBP antagonist is present in an
amount of about 0.1-100 mg/kg body weight.
 - 15 4. The method according to claim 1, in which the HBP antagonist is present in an
amount of about 0.5-50 mg/kg body weight.
 5. The method according to claim 1, in which the HBP antagonist is present in an
20 amount of about 1-25 mg/kg body weight.
 6. The method according to claim 1, in which the disorder is selected from the group
consisting of systemic inflammatory response syndrome, ischemia reperfusion,
anaphylaxis and allograft rejection.
 - 25 7. The method according to claim 1, in which the disorder is adult respiratory
distress syndrome.
 8. A method for preventing or treating a disorder resulting from release of bradykinin
30 in a mammal, wherein said mammal produces HBP that binds to aprotinin or an

analog thereof, said method comprising administering to said mammal in need thereof, aprotinin or analog thereof, in an amount effective to decrease release of bradykinin in said mammal.

5 9. The method according to claim 8, wherein said aprotinin analog is an aprotinin variant containing at least one mutation in the 15-19 position.

10. The method according to claim 8, in which the disorder is selected from the group consisting of systemic inflammatory response syndrome, ischemia reperfusion
10 anaphylaxis and allograft rejection.

11. The method according to claim 8, in which the disorder is adult respiratory distress syndrome.

15 12. A method for preventing or treating a disorder resulting from release of bradykinin in a mammal, wherein said mammal produces HBP that binds to a monoclonal antibody that binds at least one epitope of HBP, wherein said epitope binds to prekallikrein-H-kininogen complex and activates release of bradykinin, said method comprising administering to said mammal in need thereof, a monoclonal
20 antibody that binds at least one epitope of HBP, wherein said epitope binds to prekallikrein-H-kininogen complex and activates release of bradykinin, in an amount effective to decrease release of bradykinin in said mammal.

13 The method according to claim 12, wherein said mammal is a human patient
25 and said HBP is human HBP.

14. ~~The method according to claim 12, wherein said monoclonal antibody is a human monoclonal antibody.~~

15. A method of identifying an antagonist of HBP, said method comprising (a) culturing endothelial cells in the presence of HBP and in the presence and absence of a substance suspected of being said antagonist and (b) detecting any effect of said substance on permeability of endothelial cells, wherein decreased permeability of said endothelial cells as compared to permeability of said cells when incubated in the presence of HBP without said substance indicates that said substance is an antagonist.
16. The method according to claim 15, wherein in step (a) endothelial cells are first cultured in the presence of HBP and permeability of said cells are measured and then said cells are subsequently cultured in the presence of said substance.
17. The method according to claim 15, wherein in step (a), endothelial cells are first cultured in the presence of said substance and then said cells are subsequently cultured in the presence of said HBP.
18. The method according to claim 15, wherein one sample of endothelial cells are cultured in the presence of HBP and a second sample is cultured in the presence of HBP and said substance.
19. The method according to claim 15, in which the mammalian HBP is a human HBP.
20. A method for identifying a HBP antagonist comprising (a) incubating HBP with a first substance that interacts with HBP and a second substance suspected of being a HBP antagonist and (b) detecting any effect of said second substance suspected of being an antagonist on interaction of HBP with said first substance, wherein decreased interaction between said HBP with said first substance is an indication that said second substance is an HBP antagonist.

21. A method of identifying a monoclonal antibody that binds to at least one epitope on native HBP, wherein said epitope binds to prekallikrein-H-kininogen complex and activates release of bradykinin, said method comprising (a) culturing endothelial cells in the presence of HBP and in the presence and absence of a substance suspected of being said antagonist and (b) detecting any effect of said substance on permeability of endothelial cells, wherein decreased permeability of said endothelial cells as compared to permeability of said cells when incubated in the presence of HBP without said substance indicates that said monoclonal antibody binds to at least one epitope of HBP.

22. The method according to claim 21, wherein said native HBP is a human HBP.

23. A method of identifying a monoclonal antibody that binds to at least one epitope on native HBP, wherein said epitope binds to prekallikrein-H-kininogen complex and activates release of bradykinin, said method comprising (a) incubating a prekallikrein-H-kininogen complex in the presence of HBP and in the presence and absence of a monoclonal antibody suspected of binding to at least one epitope on said HBP and (b) detecting any effect of said antibody on release of bradykinin, decreased bradykinin release indicating that said antibody binds to at least one epitope on said HBP.

24. The method according to claim 23, wherein the prekallikrein-H-kininogen complex is attached to a solid support.

25. The method according to claim 23, which further comprises incubating the mixture of step (a) in the presence of endothelial cells.

26. The method according to claim 23, which further comprises incubating the mixture of step (a) in the presence of platelets.

27. The method of claim 23, wherein the native HBP is native human HBP.

28. The method according to claim 23, wherein the release of bradykinin is detected by an immunoassay.

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29. A method for determining if a mammal produces HBP that binds to an HBP antagonist comprising (a) isolating HBP or cells or tissue producing HBP from a patient; (b) incubating said HBP or cells or tissue producing HBP with a substance, tissue, cells or component thereof which interacts with HBP and said HBP antagonist and (c) detecting an effect of said HBP antagonist on the interaction of HBP with said substance, tissue, cells or components thereof, decreased interaction indicating that said HBP binds to said HBP antagonist.

30. The method according to claim 29, wherein said HBP is first incubated with
15 said antagonist, then subsequently incubated with a substance, tissue, cells or
component thereof which interacts with HBP.

31. The method according to claim 29, wherein said HBP is first incubated with a substance, tissue, cells or component thereof which interacts with HBP and then with said antagonist.

32. A test kit comprising (a) HBP antagonist; (b) HBP or cell producing HBP and (c) a substance, tissue, cells or component thereof which interact with HBP.

25 33. The test kit according to claim 32, wherein the HBP is labeled.

34. The test kit according to claim 32, wherein the test kit comprises a substance which interacts with HBP.

30 35. The test kit according to claim 32, wherein the substance is H-kininogen

36. The test kit according to claim 32, wherein the substance is labeled.

37. The test kit according to claim 30, which further comprises beads.

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38. A method for determining if a mammal produces HBP that binds to a monoclonal antibody that binds to at least one epitope on native HBP, wherein said epitope binds to prekallikrein-H-kininogen complex and activates release of bradykinin, comprising (a) isolating HBP or cells or tissue producing HBP from said mammal; (b) culturing said HBP or cells or tissue producing HBP with endothelial cells in the presence or absence of said antibody and (c) detecting any effect of said antibody on permeability of endothelial cells, decreased permeability indicating that said HBP binds to said antibody.

15 39. The method according to claim 38, in which the mammal is a human patient.

40. The method according to claim 38, wherein the native HBP is native human HBP.

20 41. A method for determining if a mammal produces HBP that binds to a monoclonal antibody that binds to at least one epitope on native HBP, wherein said epitope binds to prekallikrein-H-kininogen complex and activates release of bradykinin, comprising (a) isolating HBP or cells or tissue producing HBP from said mammal; (b) incubating said HBP or cells or tissue producing HBP with
25 prekallikrein-kininogen complex and (c) detecting any effect of said HBP on the release of bradykinin from the prekallikrein-H-kininogen complex, decreased release of bradykinin indicating that said HBP binds to said antibody.

42. A test kit comprising (a) a monoclonal antibody that binds to an epitope of HBP (b) native human HBP and (c) a prekallikrein-H-kininogen complex attached to a solid support.

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